L Number	Hits	Search Text	DB	Time stamp
1	29	antibody same (nucleic or DNA) same (benzoyl or isobutyryl or dimethoxytrityl)	USPAT; US-PGPUB; EPO; DERWENT	2004/10/26 09:02

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FILE 'USPATFULL' ENTERED AT 08:41:37 ON 26 OCT 2004
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=> DNA and antibody and (benzoyl or isobutryl or isopropylphenoxyacetyl)
L1          32 FILE CAPLUS
L2           9 FILE BIOSIS
L3          11 FILE MEDLINE
L4          11 FILE EMBASE
L5        4611 FILE USPATFULL

TOTAL FOR ALL FILES
L6        4674 DNA AND ANTIBODY AND (BENZOYL OR ISOBUTRYL OR ISOPROPYLPHENOXYAC
               ETYL)

=> dup rem
ENTER L# LIST OR (END):l1-l4
PROCESSING COMPLETED FOR L1
PROCESSING COMPLETED FOR L2
PROCESSING COMPLETED FOR L3
PROCESSING COMPLETED FOR L4
L7           47 DUP REM L1-L4 (16 DUPLICATES REMOVED)

=> l7 and (2' or 3' or pyrimidine or purine)
L8          32 S L7
L9           7 FILE CAPLUS
L10          5 S L7
L11          0 FILE BIOSIS
L12          5 S L7
L13          0 FILE MEDLINE
L14          5 S L7
L15          2 FILE EMBASE
L16          0 S L7
L17          0 FILE USPATFULL

TOTAL FOR ALL FILES
L18          9 L7 AND (2' OR 3' OR PYRIMIDINE OR PURINE)

=> d l18 ibib abs total

L18  ANSWER 1 OF 9  CAPLUS  COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER:         2004:252624  CAPLUS
DOCUMENT NUMBER:          140:303678
TITLE:                    Preparation of imidazopyridines as modulators for the
                          IgE immune response in the treatment of allergic and
                          proliferative diseases
INVENTOR(S):              Sircar, Jagadish C.; Thomas, Richard J.; Richards,
                          Mark L.; Sinha, Anjana
PATENT ASSIGNEE(S):       Avanir Pharmaceuticals, USA
SOURCE:                   PCT Int. Appl., 167 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
```

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

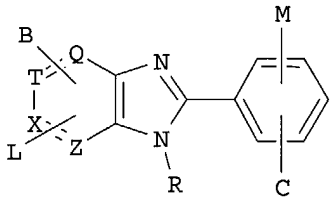
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004024897	A2	20040325	WO 2003-US30962	20030912
WO 2004024897	A3	20040826		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

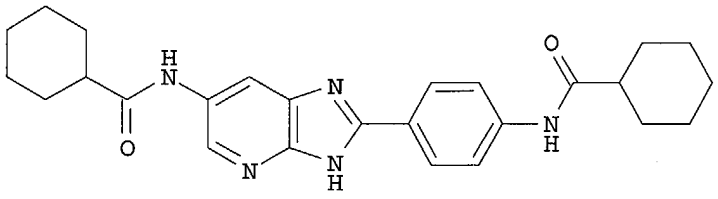
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2004116466	A1	20040617	US 2003-661296	20030912
PRIORITY APPLN. INFO.:			US 2002-410761P	P 20020912

OTHER SOURCE(S): MARPAT 140:303678
GI



I



II

AB Compds. I [A = H, halogen, R1NHCO; B = (A)n, R1NHCO, R1CONH; C = R2CONH, R2NHCO; L, M = H, (un)substituted alkyl or aryl, alkoxy, amino, alkylamino, halogen, hydroxy, nitro, cyano, trifluoromethyl, trifluoromethoxy, (un)substituted aminocarbonyl; n = 1-4; Q, T, X, Z = C, N (one of Q, T, X, Z is N); R = H, alkyl, benzyl, 4-fluorobenzyl, (dialkylamino)alkyl; R1, R2 = H, (un)substituted alkyl, cycloalkyl, Ph, naphthyl, heteroaryl] such as II are prepared as inhibitors of IgE-mediated immune response for the treatment of allergies (particularly asthma) and proliferative diseases such as cancer; I are also prepared to suppress cytokines and leukocytes. Amination of **2**-chloro-**3**,5-dinitropyridine, reduction of the 3-nitro group with ammonium sulfide, addition of 4-nitrobenzaldehyde, reduction of the nitro groups by hydrogenation with palladium on carbon, and acylation of the free amines with cyclohexanecarbonyl chloride yields II. Compds. of the invention suppress the IgE immune response by 50% at concns. between 100 μM and 1 pM (no data). Methods for the preparation of the imidazopyridine invention compds. are also claimed.

L18 ANSWER 2 OF 9 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2004:162444 CAPLUS

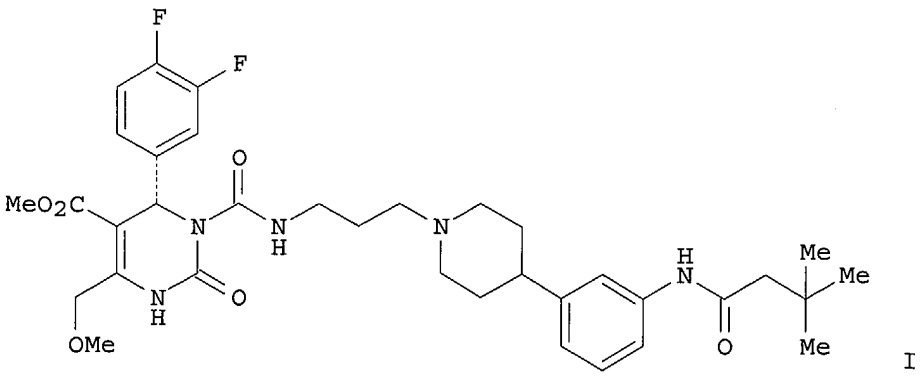
DOCUMENT NUMBER: 140:212060
TITLE: **DNA** encoding a human melanin concentrating hormone receptor (MCH1) and uses thereof and preparation of 4-phenylpiperidine derivatives as human MCH1 receptor antagonists
INVENTOR(S): Salon, John A.; Laz, Thomas M.; Nagorny, Raisa; Wilson, Amy E.; Craig, Douglas A.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 180 pp., Cont.-in-part of U.S. Ser. No. 899,732.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004038855	A1	20040226	US 2003-341751	20030114
WO 2000039279	A2	20000706	WO 1999-US31169	19991230
WO 2000039279	A3	20001102		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 2003082623	A1	20030501	US 2001-899732	20010705
WO 2004064774	A2	20040805	WO 2004-US724	20040114
W: AE, AE, AG, AL, AL, AM, AM, AM, AT, AT, AU, AZ, AZ, BA, BB, BG, BG, BR, BR, BW, BY, BY, BZ, BZ, CA, CH, CN, CN, CO, CO, CR, CR, CU, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EC, EE, EE, EG, ES, ES, FI, FI, GB, GD, GE, GE, GH, GM, HR, HR, HU, HU, ID, IL, IN, IS, JP, JP, KE, KE, KG, KG, KP, KP, KP, KR, KR, KZ, KZ, KZ, LC, LK, LR, LS, LS, LT, LU, LV, MA, MD, MD, MG, MK, MN, MW, MX, MX, MZ, MZ, NA, NI				

PRIORITY APPLN. INFO.:

WO 1999-US31169	A2	19991230
US 2000-610635	B2	20000705
US 2001-899732	A2	20010705
US 1998-224426	A2	19981231
US 2003-341751	A	20030114

GI



I

AB This invention provides an isolated nucleic acid encoding a human MCH1

receptor, a purified human MCH1 receptor, vectors comprising isolated nucleic acid encoding a human MCH1 receptor, cells comprising such vectors, **antibodies** directed to a human MCH1 receptor, nucleic acid probes useful for detecting nucleic acid encoding human MCH1 receptors, antisense oligonucleotides complementary to unique sequences of nucleic acid encoding human MCH1 receptors, transgenic, nonhuman animals which express **DNA** encoding a normal or mutant human MCH1 receptor, methods of isolating a human MCH1 receptor, methods of treating an abnormality that is linked to the activity of a human MCH1 receptor, as well as methods of determining binding of compds. to mammalian MCH1 receptors. This invention further provides a method of treating a subject suffering from urinary incontinence which comprises administering to the subject an amount of an MCH1 antagonist effective to treat the subject's urinary incontinence or overactive bladder. Various 4-phenylpiperidine derivs., e.g (I), were synthesized and tested as human MCH1 receptor antagonists.

L18 ANSWER 3 OF 9 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:695962 CAPLUS
DOCUMENT NUMBER: 137:232680
TITLE: Preparation of aryl and heteroaryl urea selective Chk1 inhibitors for use as radiosensitizers and chemosensitizers for treating diseases and conditions related to **DNA** damage or lesions in **DNA** replication
INVENTOR(S): Keegan, Kathleen S.; Kesicki, Edward A.; Gaudino, John Joseph; Cook, Adam Wade; Cowen, Scott Douglas; Burgess, Laurence Edward
PATENT ASSIGNEE(S): Icos Corporation, USA
SOURCE: PCT Int. Appl., 236 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2002070494	A1	20020912	WO 2002-US6452		20020301
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
US 2003069284	A1	20030410	US 2002-87715		20020301
EP 1379510	A1	20040114	EP 2002-728396		20020301
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR					
JP 2004523568	T2	20040805	JP 2002-569814		20020301
NO 2003003858	A	20031010	NO 2003-3858		20030901
PRIORITY APPLN. INFO.:			US 2001-273124P	P	20010302
			WO 2002-US6452	W	20020301

OTHER SOURCE(S): MARPAT 137:232680
AB Aryl- and heteroaryl substituted urea compds. (W'NHC(:Y')N(R13)Z'; 1) useful in the treatment of diseases and conditions related to **DNA** damage or lesions in **DNA** replication are disclosed. In 1, W' is a six-membered aromatic ring containing at least 2 nitrogen atoms (e.g. pyrazinyl, pyrimidinyl, pyridazinyl, 1,2,4-triazinyl, quinoxalinyl) and optionally substituted as defined in the claims, Z' is a five- or six membered aromatic or heteroarom. ring as defined in the claims, Y' is O or S. The first claim contains a much more general formula WX1C(:Y)X2Z (e.g. X1

= null, O, S, CH2, NR1; X2 = O, S, NR1) but emphasis is on 1. Methods of making the compds., and their use as therapeutic agents, for example, in treating cancer and other diseases characterized by defects in **DNA** replication, chromosome segregation, or cell division also are described. Although the methods of preparation are not claimed, about 200 example prepns. are included. N-(2-methoxy-5-methylphenyl)-N'-(2-pyrazinyl)urea and N-(4-chloro-2-methoxyphenyl)-N'-(2-pyrazinyl)urea enhanced the killing of various human cells by 5-fluorouracil from 2- to 10-fold; in HeLa cells, these same compds. enhanced killing by irradiation **2-3** fold.

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 4 OF 9 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:294160 CAPLUS
DOCUMENT NUMBER: 136:308539
TITLE: **Antibodies** to protecting groups for determination of the purity of chemically synthesized nucleic acids
INVENTOR(S): Agris, Paul F.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 28 pp., Cont.-in-part of U.S. Ser. No. 476,975.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002045167	A1	20020418	US 2000-747467	20001222
US 2003044831	A1	20030306	US 2002-190795	20020708
PRIORITY APPLN. INFO.:			US 1999-476975	A2 19991231
			US 2000-747467	A1 20001222

OTHER SOURCE(S): MARPAT 136:308539
AB This application describes an **antibody** that specifically binds to a synthetic oligomer (e.g., an oligonucleotide or oligopeptide) having a organic protecting group covalently bound thereto, which **antibody** does not bind to that synthetic oligomer when the organic protecting group is not covalently bound thereto. Methods of making and using such **antibodies** are also disclosed, along with cells for making such **antibodies** and articles carrying immobilized oligomers that can be used in assay procedures with such **antibodies**.

L18 ANSWER 5 OF 9 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:752824 CAPLUS
DOCUMENT NUMBER: 135:314438
TITLE: Proteolipid subunits of vacuolar H+-ATPase (ATP6F) as tumor antigens, application to cancer therapy, and use of proton pump inhibitor as anticancer agent
INVENTOR(S): Sato, Nobuo; Suzuki, Nobutaka; Yamaguchi, Masaaki; Yamaguchi, Nobuo; Okuma, Katsuji
PATENT ASSIGNEE(S): Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 79 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2001286284	A2	20011016	JP 2000-103966	20000405

PRIORITY APPLN. INFO.: JP 2000-103966 20000405

AB Proteolipid subunits of vacuolar H+-ATPase (V-ATPase) as tumor antigens, use of **antibodies** and antisense oligonucleotides targeting those antigens as anticancer agent, and use of proton pump inhibitor as anticancer agent, are disclosed. Tumor antigen recognized by monoclonal **antibody** KCT-1 was isolated from thyroid cancer cell line TPC-1. The amino acid sequence of this antigen named SSY (S-1) was found match that of vacuolar H+-ATPase proteolipid subunit (ATP6F, c'' subunit). The epitope of SSY antigen for KCT-1 **antibody** was determined SSY antigen was found to strongly expressed in all the cancers examined; thyroid cancer, breast cancer, stomach cancer, esophagus cancer (squamous cell carcinoma), laryngeal cancer, colon cancer, rectal cancer, anal cancer, pancreatic cancer, lung cancer, renal cancer, bladder cancer, ovarian cancer, uterus cancer, cervical cancer, cunnus cancer, skin cancer, melanoma, central or peripheral nervous system cancer, gingival cancer, pharyngeal carcinoma, mediastinal tumor, liver cancer, bile duct cancer (cholangioma), gallbladder cancer, renal pelvis tumor, ureter cancer, testicular cancer, fallopian tube cancer, vaginal cancer, sarcoma, leukemia, erythroleukemia, multiple myeloma, malignant lymphoma, and carcinosarcoma. CDNA for a mouse homolog was cloned. Intradermal, s.c., and oral administration of the antigen in mouse demonstrated antitumor activity and safety. Antitumor activity was also demonstrated by phosphorothioate antisense oligonucleotide. Various inhibitors of V-ATPase, H+/K+-ATPase, and H+/Cl- symporter were found to have antitumor activity.

L18 ANSWER 6 OF 9 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2000:405009 CAPLUS

DOCUMENT NUMBER: 133:172107

TITLE: Antagonist effects on human P2X7 receptor-mediated cellular accumulation of YO-PRO-1

AUTHOR(S): Michel, A. D.; Kaur, R.; Chessell, I. P.; Humphrey, P. P. A.

CORPORATE SOURCE: Glaxo Institute of Applied Pharmacology, Department of Pharmacology, University of Cambridge, Cambridge, CB2 1QJ, UK

SOURCE: British Journal of Pharmacology (2000), 130(3), 513-520
CODEN: BJPCBM; ISSN: 0007-1188

PUBLISHER: Nature Publishing Group

DOCUMENT TYPE: Journal

LANGUAGE: English

AB 1 The authors have examined the interaction of P2 antagonists with the human P2X7 receptor by studying their effect on **2'** and **3'**-O-**benzoyl-benzoyl**-ATP (DbATP) stimulated cellular accumulation of the fluorescent, **DNA** binding dye, YO-PRO-1 (MW = 375 Da). 2 In suspensions of HEK293 cells expressing human recombinant P2X7 receptors, DbATP produced time and concentration-dependent increases in YO-PRO-1 fluorescence. This response presumably reflects YO-PRO-1 entry through P2X7 receptor channels and binding to nucleic acids. When studies were performed in a NaCl-free, sucrose-containing buffer, full concentration-effect curves to DbATP could be constructed. 3 The P2 antagonists, pyridoxalphosphate-6-azophenyl-2',4'-disulfonic acid (PPADS) and periodate oxidized ATP (oATP), reduced the potency of DbATP and decreased its maximum response. 1-[N,O-bis(1,5-isoquinolinesulfonyl)-N-methyl-L-tyrosyl]-4-phenylpiperazine (KN62) and its analog, KN04, reduced the potency of DbATP. Schild slopes for KN62 and KN04 were shallow and exhibited a plateau at concns. of compound greater than 1 μM, indicating that these compds. were not competitive antagonists. 4 Calmidazolium and a monoclonal **antibody** to human P2X7 receptors attenuated DbATP-stimulated YO-PRO-1 accumulation but they were not competitive antagonists and only produced **2-3** fold decreases in the potency of DbATP. 5 The effects of PPADS and KN62 were partially reversible whereas those of oATP were not. PPADS protected cells against

the irreversible antagonist effects of oATP suggesting a common site of action. In contrast KN62 was not effective suggesting that it may bind at a different site to oATP and PPADS. 6 This study has demonstrated that P2X7 receptor function can be quantified by measuring DbATP stimulated YO-PRO-1 accumulation and has provided addnl. information about the interaction of P2 receptor antagonists with the human P2X7 receptor.
REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 7 OF 9 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:461766 CAPLUS
DOCUMENT NUMBER: 129:272140
TITLE: The terminal O-acetyltransferase involved in vindoline biosynthesis defines a new class of proteins responsible for coenzyme A-dependent acyl transfer
AUTHOR(S): St-Pierre, Benoit; Laflamme, Pierre; Alarco, Anne-Marie; De Luca, Vincenzo
CORPORATE SOURCE: Institut de Recherche en Biologie Vegetale, Departement de Sciences Biologiques, Universite de Montreal, Montreal, QC, H1X 2B2, Can.
SOURCE: Plant Journal (1998), 14(6), 703-713
CODEN: PLJUED; ISSN: 0960-7412
PUBLISHER: Blackwell Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The gene encoding acetyl CoA:deacetylvindoline 4-O-acetyltransferase (DAT) (EC **2.3**.1.107) which catalyzes the last step in vindoline biosynthesis was isolated and characterized. The genomic clone encoded a 50-kDa polypeptide containing the sequences of nine tryptic fragments derived from the purified DAT heterodimer. However, cleavage of DAT protein to yield a heterodimer appears to be an artifact of the protein purification procedure, since the size of the protein (50 kDa) cross-reacting with anti-DAT **antibody** in seedlings and in leaves of various ages also corresponds to the size of the active recombinant enzyme. Studies with the intact plant and with developing seedlings showed that induction of DAT mRNA, protein accumulation and enzyme activity occurred preferentially in vindoline producing tissues such as leaves and cotyledons of light-treated etiolated seedlings. The ORF of DAT showed significant sequence identity to 19 other plant genes, whose biochem. functions were mostly unknown. The Mr of ≈50 kDa, a HXXXDG triad, and a DFGWGKP consensus sequence are highly conserved among the 20 plant genes and these criteria may be useful to identify this type of acyltransferase. The involvement of some of these genes in epicuticular wax biosynthesis, fruit-ripening and in **benzoyl** -transfer reactions indicates that the plant kingdom contains a superfamily of multifunctional acyltransferases which operate by a reaction mechanism related to the ancient chloramphenicol O-acetyltransferase and dihydrolipoyl acetyltransferase class of enzymes.
REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 8 OF 9 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 2001151361 EMBASE
TITLE: Expression of a P2X(7) receptor by a subpopulation of human osteoblasts.
AUTHOR: Gartland A.; Hipskind R.A.; Gallagher J.A.; Bowler W.B.
CORPORATE SOURCE: A. Gartland, Human Anatomy and Cell Biology Group, Dept. of Hum. Anat. and Cell Biology, University of Liverpool, Ashton Street, Liverpool L69 3GE, United Kingdom
SOURCE: Journal of Bone and Mineral Research, (2001) 16/5 (846-856).
Refs: 41
ISSN: 0884-0431 CODEN: JBMREJ

COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English

AB There is now conclusive evidence that extracellular nucleotides acting via cell surface P2 receptors are important local modulators of bone cell function. Multiple subtypes of P2 receptors have been localized to bone, where their activation modulates multiple processes including osteoblast proliferation, osteoblast-mediated bone formation, and osteoclast formation and resorptive capacity. Locally released nucleotides also have been shown to sensitize surrounding cells to the action of systemic factors such as parathyroid hormone (PTH). In nonskeletal tissue recent attention has focused on one particular P2 receptor, the P2X(7) receptor (previously termed P2Z), and its ability to form nonselective aqueous pores in the plasma membrane on prolonged stimulation. Expression of this receptor originally was thought to be restricted to cells of hemopoietic origin, in which it has been implicated in cell fusion, apoptosis, and release of proinflammatory cytokines. However, recent reports have indicated expression of this receptor in cells of stromal origin. In this study, we investigated the expression of the P2X(7) receptor in two human osteosarcoma cell lines, as well as several populations of primary human bone-derived cells (HBDCs) at the levels of messenger RNA (mRNA) and protein. We found that there is a subpopulation of osteoblasts that expresses the P2X(7) receptor and that these receptors are functional as assessed by monitoring ethidium bromide uptake following pore formation. Inhibition of delayed lactate dehydrogenase (LDH) release in response to the specific agonist **2',3'**-(4-**benzoyl**)-**benzoyl**-adenosine triphosphate (BzATP) by the nonspecific P2X receptor antagonist PPADS confirmed a receptor-mediated event. After treatment with BzATP SaOS-2 cells exhibited dramatic morphological changes consistent with those observed after P2X(7)-mediated apoptosis in hemopoietic cells. Dual staining with terminal deoxynucleotidyl transferase-mediated deoxyuridine triphosphate-biotin nick end labeling (TUNEL) and a P2X(7)-specific monoclonal **antibody** confirmed the induction of apoptosis in osteoblasts expressing the P2X(7) receptor. These data show for the first time the expression of functional P2X(7) receptors in a subpopulation of osteoblasts, activation of which can result in ATP-mediated apoptosis.

L18 ANSWER 9 OF 9 EMBASE
on STN
ACCESSION NUMBER: 1998063019 EMBASE
TITLE: Continuing the fight against advanced colorectal cancer: New and future treatment options.
AUTHOR: Bleiberg H.
CORPORATE SOURCE: H. Bleiberg, Chemotherapy/Gastroenterology Unit, Institut Jules Bordet, rue Heger Bordet, 100 Brussels, Belgium
SOURCE: Anti-Cancer Drugs, (1998) 9/1 (18-28).
Refs: 83
ISSN: 0959-4973 CODEN: ANTDEV
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 016 Cancer
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English

AB The benefit of chemotherapy in the treatment of advanced colorectal cancer has now been clearly demonstrated with several studies reporting advantages in terms of overall survival, quality of life and effective palliation following chemotherapy plus supportive care in comparison to supportive care alone. However, the survival benefit achieved with the

current 5-fluorouracil (5-FU)-based regimens is modest and thus investigations are ongoing to identify more effective agents with novel mechanisms of action. The three new agents likely to have the greatest impact in the near future are the thymidylate synthase inhibitor ZD1694 (Tomudex®), the topoisomerase I inhibitor irinotecan (Campto®) and the new platinum compound, oxaliplatin (L-OHP®). Promising response rates of 26 and 20% have been reported with ZD1694 in patients with advanced colorectal cancer in phase II and III studies, respectively. In a European phase II study, irinotecan has achieved response rates of 19% in chemotherapy-naive patients and 18% in pretreated patients with advanced disease. Oxaliplatin has mainly been investigated in combination with continuous infusion 5-FU, with response rates of 29-58%. Other agents currently in development include monoclonal **antibodies** (e.g. 17-1A and MN-14), protein synthesis inhibitors (e.g. RA 700) and angiogenesis inhibitors (e.g. PF 4).